Medical Image Processing, Analysis & Visualization In Clinical Research

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Abstract

Imaging has become an essential component in many fields of medical and laboratory research and clinical practice. Biologists study cells and generate 3D confocal microscopy datasets, virologists generate 3D reconstructions of viruses from micrographs, radiologists identify and quantify tumors from MRI and CT scans, and neuroscientists detect regional metabolic brain activity from PET and functional MRI scans. Analysis of these diverse image types requires sophisticated computerized quantification and visualization tools. Until recently, three-dimensional visualization of images and quantitative analysis could only be performed using expensive UNIX workstations and customized software. Today, much of the visualization and analysis can be performed on an inexpensive desktop computer equipped with the appropriate graphics hardware and software. This paper introduces an extensible platform-independent, general-purpose image processing and visualization program specifically designed to meet the needs of a Internet-linked medical research community. The application named MIPAV (Medical Image Processing Analysis and Visualization) enables clinical and quantitative analysis of medical images over the Internet. Using MIPAV's standard user-interface and analysis tools, researchers and clinicians at remote sites can easily share research data and analyses, thereby enhancing their ability to study, diagnose, monitor, and treat medical disorders.

1. Introduction

We have developed a general-purpose, extensible image processing and visualization program to facilitate imaging research at the NIH. MIPAV, an acronym for Medical Image Processing Analysis and Visualization, is n-dimensional, platform-independent, and can process data originating from most medical imaging modalities. The program functions both as an end-user application and an Application Programming Interface (API) that can be used to develop other image processing, registration, and visualization applications. As an end-user application, it provides a numerous basic and sophisticated image analysis and visualization tools. Researchers who possess knowledge of basic programming skills and image processing can use MIPAV as an API to build customized analysis or visualization components through MIPAV's plug-in feature.

2. Overall Design

MIPAV, written in the Java programming language, is modular in design, and takes advantage of Java's object-oriented features. A functional overview of MIPAV and its core features is diagrammed in Figure1. The bottom block lists a subset of currently supported file formats. Using information stored in the file header, images are read into the appropriate data-type buffer. The data-type buffer is n-dimensional, but typically, images up to four dimensions are stored and processed. In addition, the buffer also stores all native and many extended data types (boolean, byte, unsigned byte, short, unsigned short, integer, long, float, double, RGB, and complex). Three functional blocks interface with the data buffer (or image model): the Views, VOIs, and Algorithms. The "Views" interface provides the user with a graphical user interface to view and manipulate the image and associated structures (i.e. VOIs). The VOI's module enables interactive segmentation and measurement. The Algorithms module contains over 20 image processing and analysis tools. The functionality of these modules is distributed over an intuitive user interface.

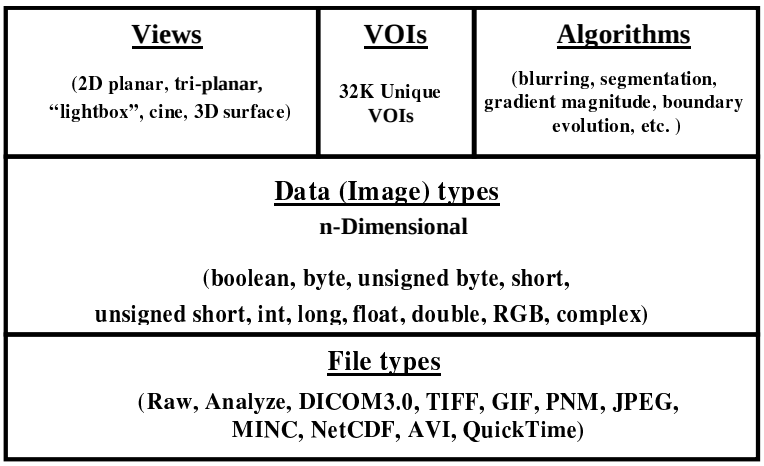

Figure 1. Functional overview of MIPAV's design.

MIPAV was specifically designed for the NIH intramural research community imaging requirements which include:

a. Cross-platform or platform-independent execution

As mentioned above, much of NIH's research involves the segmentation, quantification, and visualization of 2D, 3D and 4D image datasets, including but not limited to microscopy, microarray data, X-ray, computed tomography (CT), magnetic resonance imaging (MRI), functional MRI (fMRI) and PET. Factors such as personal preference, data requirements, software limitations, and precedent have led to a heterogeneous distribution of computer platforms, among which are PCs executing Windows or Linux, Macintoshes, and workstations by SGI, Sun Microsystems, and Hewlett Packard. Furthermore, the analysis of some image datasets may require multiple types of computers to accommodate the required (non-MIPAV) analysis software packages that only execute on specific platforms or operating systems. In order to consolidate the functionality of these separate programs into an integrated package that runs on available hardware one must adopt platform-independent software.

In short, platform-independent software abstracts the underlying hardware and provides a common virtual platform. Software written for this virtual platform automatically runs on a many different types of computers significantly decreasing hardware and software development and maintenance costs.

b. Access to images - DICOM 3.0 files/server, Analyze, TIFF, Raw, etc.

Before one can perform image analysis and quantification, an application must seamlessly be able to access, read and write image datasets in industry-standard formats. Conformance to accepted standards (i.e. DICOM, TIFF etc.) ensures compatibility with present and future applications and medical equipment. This in turn protects the researcher's investment in hardware and provides flexibility in reaching their goals.

One of MIPAV's strengths is its ability to access medical images via the DICOM query and retrieve module. MIPAV is DICOM compliant[2] and is able to retrieve images from the NIH Clinical Center's PACS system, a DICOM server located on the imaging device (i.e. CT or MRI machine), or any other DICOM compliant server (Figure 2). Most importantly, MIPAV provides remote access to clinical images via the DICOM interface. The researcher can access, display and analyze images from a computer in an office or any location where there is access to the Internet.

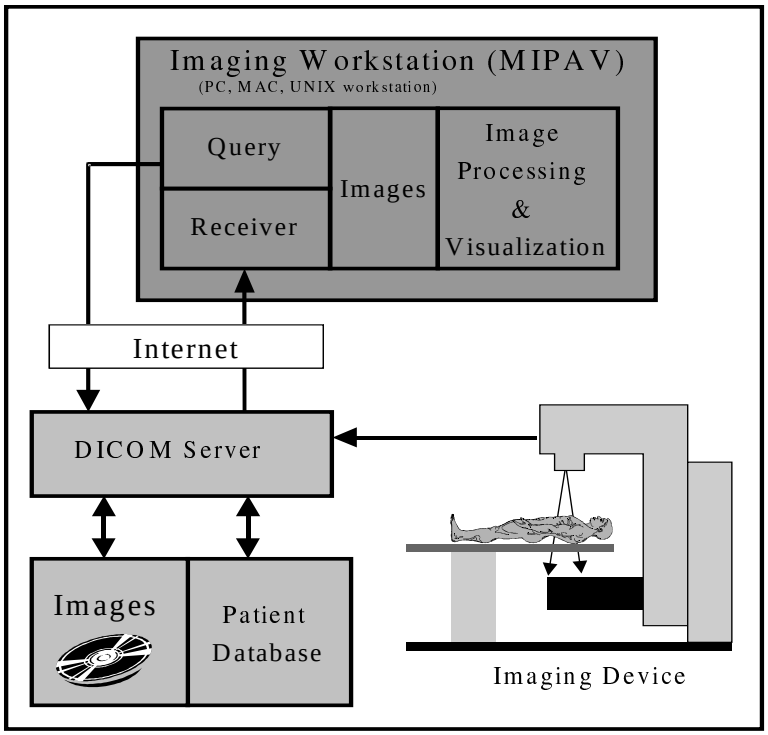

Figure 2. DICOM query/retrieve block diagram.

c. Volume Of Interest (VOI) - automatic generation (i.e. segmentation), manual correction, and quantification

Image segmentation is the process of identifying *connected* regions of images as members of a common group that can be delineated by VOI structures. In the medical

field, physicians routinely identify (i.e. segment) structures in medical images to facilitate the treatment of patients. For example, many researchers studying the brain are interested in the segmentation of gray matter, white matter, and cerebrospinal fluid in magnetic resonance images[1]. The quantification of these various tissue types enables researchers to better understand, diagnose, monitor and treat neurobehavioral disorders.

Using the MIPAV application, VOI generation (segmentation) can be automatic, semi-automatic or user-guided, manual or some combination of these types. The image data type and segmentation task guide the selection of an image segmentation method from the many available in MIPAV. Automatic segmentation methods are desirable because they require no user interaction that can be subject to operator error and decreased reliability. However, results from automatic segmentation sometime require manual VOI correction (adjustment of the boundary which identifies the region). MIPAV also enables the user to apply custom segmentation algorithms and the calculation of VOI statistics such as: area/volume, orientation, number of pixels, center of mass, average density.

d. Extensibility – plug-in and macro capability

MIPAV is an analysis and visualization application that has been developed to satisfy a broad range of researcher requirements. However, there are instances when research projects require unique and specialized functionality. MIPAV meets these requirements by incorporating a plug-in architecture that enables researchers to add their own java-based image processing components. A simpler MIPAV macro language is also under development.

e. Visualization of 2D, 3D, and 4D datasets

Information contained in confocal micrographs, CT, MRI, and fMRI scans are best conveyed through a flexible and realistic 3D visualization system that combines adjacent slices into a 3D image volume. MIPAV's visualization system provides numerous tools including surface rendering, composite displays of two datasets, image magnification, rotation about an axes, color look-up tables, multi-planar views, and movies. A volume-rendering tool has been implemented and is being tested.

3. Applications of MIPAV at NIH.

3.1. Segmentation and visualization of structural and functional MRI brain images

The Geriatric Psychiatry Branch, NIMH conducts research on elderly patients diagnosed with Alzheimer's disease, first degree relatives of Alzheimer's patients, and elderly individuals who have recently lost their spouses and may be experiencing depressive symptoms. Brain changes that precede the onset of the clinical symptoms of Alzheimer's disease have been reported [3]. MIPAV's multiple layer capability is used to generate and edit VOIs, which are quantified to determine subtle changes in total brain volume and selected brain structures over a ten-year span. To measure total brain volumes, skull, meninges, sulcal CSF, and extraneous muscle tissue are first removed by drawing VOIs at difficult-to-segment brain boundaries and applying an optimized watershed segmentation algorithm (Figure 3). Second, any residual extraneous tissue is removed using the VOI editing tools and paint functions. Total brain volume measurements are then obtained using mensuration information contained in the DICOM header.

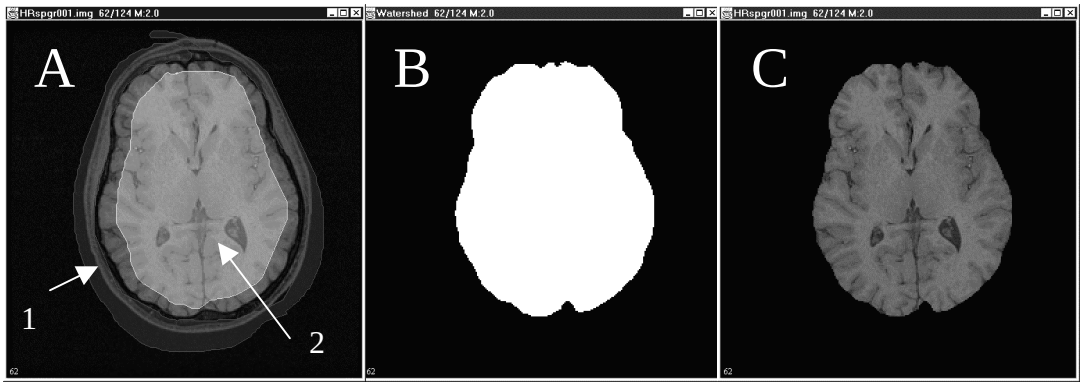

Figure 3. A. Axial image of a human brain and VOIs used for removal of skull, meninges, sulcal CSF, and extraneous muscle tissue. The VOI defining the watershed basin for tissue to be removed is drawn outside the brain (1). The VOI defining the watershed basin for tissue to be retained is drawn inside the brain (2). B. The mask generated by the watershed segmentation. C. The resulting deskulled brain after multiplying the mask and original image. No additional editing was required at this particular brain slice. This watershed segmentation method easily extends to 3-D volumes.

3.2. National Eye Institute (NEI)

The NEI is in Phase I in the evaluation of a new laser technique to slow or stop the progression of choroidal neovascularization (CNV) associated with age-related macular degeneration (AMD). AMD is a serious health problem and is the most common cause of blindness in patients over the age of 60. CNV formation in patients can be visualized with the use of fluorescein (FA) and indocyanine (ICG) angiography Because of the eye's optics, FA and ICG angiography images are typically acquired at varying angles and magnification. Additionally, FA images are captured using a 520 nM filter cutoff while ICG images are obtained with an approximate 650 nM cutoff filter and black and white images are obtained with a red-free visible wavelength filter. The NEI is evaluating the use of a targeted laser photocoagulation technique to treat CNV. This technique requires identifying CNV in images obtained through FA and ICG with treatment and treating an area on a corresponding black and white digital photograph of the eye. As such, images obtained from different imaging capturing techniques and from different angles and magnification, need to be superimposed and analyzed.

Figure 4 shows images captured at different angles and wavelengths needing registration and superimposition to accurately identify CNV. Homologous landmarks, where placed manually on the FA image (Figure 4A) and in the black and white corresponding image (Figure 4B). The images in figures 4A and 4B were registered using a least-squares registration algorithm to align the landmarks and are shown superimposed before and after registration in figures 4C and 4D, respectively [4].

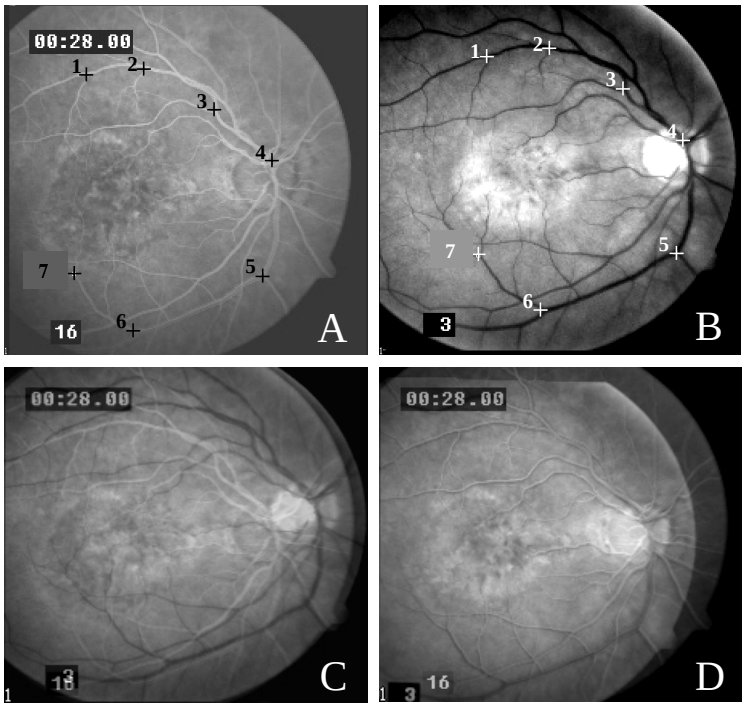

Figure 4. Images of the retina from a patient with CNV and AMD. Homologous landmarks, placed manually in A and B and are used to register the images using a Least-squares algorithm[4]. (A) Flourescein angiographic image. (B) Black and white corresponding image. (C) Unregistered images (D) Registered images.

4. Conclusions and Future Directions

Significant progress has been achieved in building a platform-independent, n-dimensional, general-purpose, extensible image processing application. However much work still remains to meet the broader needs of the NIH user community. At present, we are adding a variety of registration algorithms to MIPAV as well as surface rendering. Future enhancements will also include volume rendering, more sophisticated segmentation algorithms, and the continuous modification of specialized components to address specific requirements identified by our collaborators. Lastly, the MIPAV scripting language will enable users to automated repeated tasks. While MIPAV has primarily addressed radiological imaging modalities, it is suitable for other types of datasets including microarrays, microscopy images, and micrographs. Future enhancements will add functionality for these technologies as needed. Among the more aggressive goals is to leverage Java's distributed execution capabilities to improve algorithm performance.

5. References

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